Lys Arg

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FIGURE 1

Murine Antibody 3B9 Light Chain Native Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO:1
Amino Acid Sequence SEO ID NO:2

Ami	no A	cid :	Sequ	ence	SEQ	ID	NO: 2						
ATG Met 1	GAG Glu	ACA Thr	GAC Asp	ACA Thr 5	ATC Ile	CTG Leu	CTA Leu	TGG Trp	GTG Val 10	CTG Leu	CTG Leu	CTC Leu	39
TGG Trp	GTT Val 15	CCA Pro	GGC Gly	TCC Ser	ACT Thr	GGT Gly 20	GAC Asp	ATT Ile	GTG Val	CTG Leu	ACC Thr 25	CAA Gln	78
TCT Ser	CCA Pro	GCT Ala	TCT Ser 30	Leu	GCT Ala	GTG Val	TCT Ser	CTA Leu 35	GGG Gly	CAG Gln	AGG Arg	GCC Ala	117
ACC Thr 40	ATC Ile	TCC Ser	TGC Cys	AAG Lys	GCC Ala 45	AGC Ser	CAA Gln	AGT Ser	GTT Val	GAT Asp 50	TAT Tyr	GAT Asp	156
GGT Gly	GAT Asp	AGT Ser 55	TAT Tyr	ATG Met	AAC <u>Asn</u>	TGG Trp	TAC Tyr 60	CAA Gln	CAG Gln	AAA Lys	CCA Pro	GGA Gly 65	195
CAG Gln	CCA Pro	CÇC Pro	AAA Lys	CTC Leu 70	CTC Leu	ATC Ile	TAT Tyr	GCT Ala	GCA Ala 75	TCC Ser	AAT Asn	CTA Leu	234
GAA <u>Glu</u>	TCT Ser 80	GGG Gly	ATC Ile	CCA Pro	GCC Ala	AGG Arg 85	TTT Phe	AGT Ser	GGC Gly	AGT Ser	GGG Gly 90	TCT Ser	273
GGG Gly	ACA Thr	GAC Asp	TTC Phe 95	ACC Thr	CTC Leu	AAC Asn	ATC Ile	CAT His 100	CCT Pro	GTG Val	GAG Glu	GAG Glu	312
GAG Glu 105	GAT Asp	GCT Ala	GCA Ala	ACC Thr	TAT Tyr 110	TAC Tyr	TGT Cys	CAG Gln	CAA Gln	AGT Ser 115	AAT Asn	GAG Glu	351
GAT Asp	CCT Pro	CCG Pro 120	ACG Thr	TTC Phe	GGT Gly	GGA Gly	GGC Gly 125	ACC Thr	AAG Lys	CTG Leu	GAA Glu	ATC Ile 130	390
AAA	CGG												306

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Figure 2

Murine Antibody 3B9 Heavy Chain Native Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 3 Amino Acid Sequence SEQ ID NO: 4

GAATTCGCGG CCGCTATGCA GGGACAATCA GCAGCAGCAA													
TGAGGAAGTA AGCCTGTGCA GAT ATG AAC AGG CTT ACT TCC Met Asn Arg Leu Thr Ser 1 5													
TCA TTG CTG CTG CTG ATT GTC CCT GCA TAT GTC CTG TCC Ser Leu Leu Leu Ile Val Pro Ala Tyr Val Leu Ser 10 15	120												
CAG GTT ACT CTG AAA GAG TCT GGC CCT GGG ATA TTG CAG Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln 20 25 30	159												
CCC TCC CAG ACC CTC AGT CTG ACT TGT TCT TTC TCT GGG Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly 35 40 45	198												
TTT TCA CTG AGC ACT TCT GGT ATG GGT GTG AGC TGG ATT Phe Ser Leu Ser Thr Ser Gly Met Gly Val Ser Trp Ile 50 55	237												
CGT CAG CCT TCA GGA AAG GGT CTG GAG TGG CTG GCA CAC Arg Gln Pro Ser Gly Lys Gly Leu Glu Trp Leu Ala His 60 65 70	276												
ATT TAC TGG GAT GAT GAC AAG CGC TAT AAC CCA TCC CTG Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ser Leu 75 80	315												
AAG AGC CGG CTC ACA ATC TCC AAG GAT ACC TCC AGC AAC Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Asn 85 90 95	354												
CAG GTA TTC CTC AAG ATC ACC AGT GTG GAC ACT GCA GAT Gln Val Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp 100 105 110	393												
ACT GCC ACA TAC TAC TGT GCT CGA AGA GAG ACT GTG TTC Thr Ala Thr Tyr Tyr Cys Ala Arg Arg Glu Thr Val Phe	432												

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Figure 2 (con't)

TAC Tyr	TGG Trp	TAC Tyr	TTC Phe	GAT Asp	GTC Val	TGG Trp	GGC Glv	GCA Ala	GGG Glv	ACC	ACG Thr	GTC Val	471
	125	75.				130			1		135		
						130					133		
3.00	cma	maa	max										
		TCC											483
Thr	Val	Ser	Ser										
			140										

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FIGURE 3

Human/Murine 3B9 Chimeric Antibody Heavy Chain Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 9 Amino Acid Sequence SEQ ID NO:10

Amino Acid Sequence	SEQ ID NO:10	
	CAG GTC TTC ATT TCT CTG TTG CTC Gln Val Phe Ile Ser Leu Leu Leu 10	39
	TAC GGG CAG GTT ACC CTG AAA GAG Tyr Gly Gln Val Thr Leu Lys Glu 20 25	78
	TTG CAG CCC TCC CAG ACC CTC AGT Leu Gln Pro Ser Gln Thr Leu Ser 35	117
	TCT GGG TTT TCA CTG AGC ACT TCT Ser Gly Phe Ser Leu Ser Thr Ser 45	156
	TGG ATT CGT CAG CCT TCA GGA AAG Trp Ile Arg Gln Pro Ser Gly Lys 60 65	195
	G GCA CAC ATT TAC TGG GAT GAT GAC Ala <u>His Ile Tyr Trp Asp Asp Asp</u> 75	234
	A TCC CTG AAG AGC CGG CTC ACA ATC Ser Leu Lys Ser Arg Leu Thr Ile 85 90	273
	AGC AAC CAG GTA TTC CTC AAG ATC Ser Asn Gln Val Phe Leu Lys Ile 100	312
ACC AGT GTG GAC ACT Thr Ser Val Asp Thr 105	GCA GAT ACT GCC ACA TAC TAC TGT Ala Asp Thr Ala Thr Tyr Tyr Cys	351
	GTG TTC TAC TGG TAC TTC GAT GTC Val Phe Tyr Trp Tyr Phe Asp Val	390
	C ACG GTC ACC GTC TCC TCA T Thr Val Thr Val Ser Ser 5 140	423

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FIGURE 4

Humanized 3B9 Antibody Heavy Chain Signal Sequence and Variable Region

Nucleotide Sequence SEQ ID NO: 11 Amino Acid Sequence SEQ ID NO: 12

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t,	ATG Met 1	<i>GTG</i> Val	<i>TTG</i> Leu	<i>CAG</i> Gln	ACC Thr 5	<i>CAG</i> Gln	<i>GTC</i> Val	TTC Phe	<i>ATT</i> Ile	TCT Ser 10	<i>CTG</i> Leu	TTG Leu	<i>CTC</i> Leu	39
	TGG Trp	ATC Ile 15	TCT Ser	GGT Gly	GCC Ala	Tyr	GGG Gly 20	CAG Gln	GTT Val	ACC Thr	CTG Leu	CGT Arg 25	GAA Glu	78
	TCC Ser	GGT Gly	CCG Pro	GCA Ala 30	CTA Leu	GTT Val	AAA Lys	CCG Pro	ACC Thr 35	CAG Gln	ACC Thr	CTG Leu	ACG Thr	117
	TTA Leu 40	ACC Thr	TGC Cys	ACC Thr	TTC Phe	TCC Ser 45	GGT Gly	TTC Phe	TCC Ser	CTG Leu	TCG Ser 50	ACC Thr	TCC Ser	156
	GGT Gly	ATG Met	GGT Gly 55	GTT Val	TCC Ser	TGG Trp	ATC Ile	CGT Arg 60	CAG Gln	CCG Pro	CCG Pro	GGT Gly	AAA Lys 65	195
	GGT Gly	CTA Leu	GAA Glu	TGG Trp	CTG Leu 70	GCT Ala	CAC His	ATC Ile	TAC Tyr	TGG Trp 75	GAC Asp	GAC Asp	GAC Asp	234
	AAA Lys	CGT Arg 80	TAC Tyr	AAC Asn	CCG Pro	AGC Ser	CTG Leu 85	AAA Lys	TCC Ser	CGT Arg	CTG Leu	ACG Thr 90	ATA Ile	273
	TCC Ser	AAA Lys	GAC Asp	ACC Thr 95	TCC Ser	CGT Arg	AAC Asn	CAG Gln	GTT Val 100	GTT Val	CTG Leu	ACC Thr	ATG Met	312
	ACT Thr 105	AAC Asn	ATG Met	GAC Asp	CCG Pro	GTT Val 110	GAC Asp	ACC Thr	GCT Ala	ACC Thr	TAC Tyr 115	TAC Tyr	TGC Cys	351
	GCT Ala	CGA Arg	CGC Arg 120	GAA Glu	ACC Thr	GTT Val	TTC Phe	TAC Tyr 125	TGG Trp	TAC Tyr	TTC Phe	GAC Asp	GTT <u>Val</u> 130	390
	TGG Trp	GGT Gly	Arg	Gly	ACC Thr	Pro	GTT Val	ACC Thr	GTG Val	AGC Ser	TCA Ser			423

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CGT

Arg

393



FIGURE 5

Humani:	zed	3B9	An	tibo	ody	Light	Chain
Signal	Seg	quend	ce	and	Var	iable	Region

Nucleotide Sequence SEQ ID NO: 13 Amino Acid Sequence SEQ ID NO: 14

	•		-										
ATG Met 1	GGA Gly	TGG Trp	AGC Ser	TGT Cys 5	ATC Ile	ATC Ile	CTC Leu	TTC Phe	TTG Leu 10	GTA Val	GCA Ala	ACA Thr	39
GCT Ala	ACA Thr 15	GGT Gly	GTC Val	CAC His	TCC Ser	GAT Asp 20	ATC Ile	GTG Val	ATG Met	ACC Thr	CAG Gln 25	TCT Ser	78
CCA Pro	GAC Asp	TCG Ser	CTA Leu 30	GCT Ala	GTG Val	TCT Ser	CTG Leu	GGC Gly 35	GAG Glu	AGG Arg	GCC Ala	ACC Thr	117
ATC Ile 40	AAC Asn	TGC Cys	AAG <u>Lys</u>	GCC Ala	TCC Ser 45	CAA Gln	AGT Ser	GTT Val	GAT Asp	TAT Tyr 50	GAT Asp	GGT Gly	156
			Met	AAC Asn									195
CCT Pro	CCT Pro	AAG Lys	TTG Leu	CTC Leu 70	ATT Ile	TAC Tyr	GCT Ala	GCA Ala	TCC Ser 75	AAT Asn	CTA Leu	GAA Glu	234
TCT <u>Ser</u>	GGG Gly 80	GTA Val	CCT Pro	GAC Asp	CGA Arg	TTC Phe 85	AGT Ser	GGC Gly	AGC Ser	GGG Gly	TCT Ser 90	GGG Gly	273
ACA Thr	GAT Asp	TTC Phe	ACT Thr 95	CTC Leu	ACC Thr	ATC Ile	AGC Ser	AGC Ser 100	CTG Leu	CAG Gln	GCT Ala	GAA Glu	312
GAT Asp 105	GTG Val	GCA Ala	GTA Val	TAC Tyr	TAC Tyr 110	TGT Cys	CAG Gln	CAA Gln	AGT Ser	AAT <u>Asn</u> 115	GAG Glu	GAT Asp	351
CCT Pro	CCG Pro	AGG Arg 120	TTC Phe	GGC Gly	GGA Gly	GGG Gly	ACC Thr 125	AAG Lys	GTG Val	GAG Glu	ATC Ile	AAA Lys 130	390

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FIGURE 6A

Signal Sequ	uence	€	
Nucleotide			
Amino Acid	SEQ	ID	NO: 6

ATG GTG TTG CAG ACC CAG GTC TTC ATT TCT CTG TTG CTC
Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu
1 10

TGG ATC TCT GGT GCC TAC Trp Ile Ser Gly Ala Tyr 15

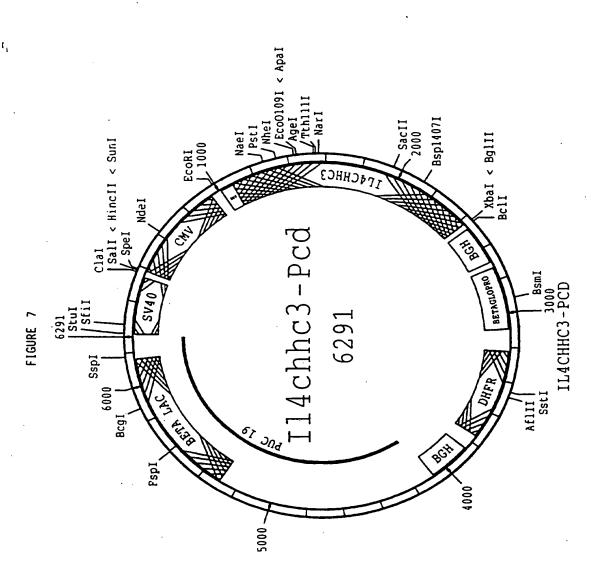
FIGURE 6B

Signal Sequence Nucleotide SEQ ID NO:7 Amino Acid SEQ ID NO:8

ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG GTA GCA ACA
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr
1 5 10

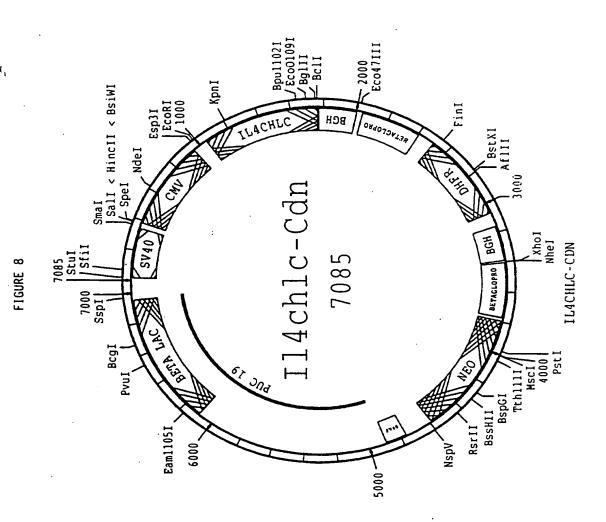
GCT ACA GGT GTC CAC TCC GAT ATC GTG ATG ACC CAG TCT 78
Ala Thr Gly Val His Ser Asp
15 20

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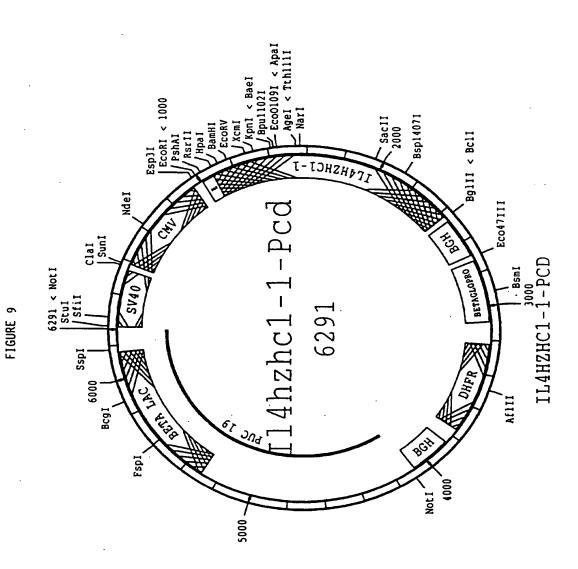


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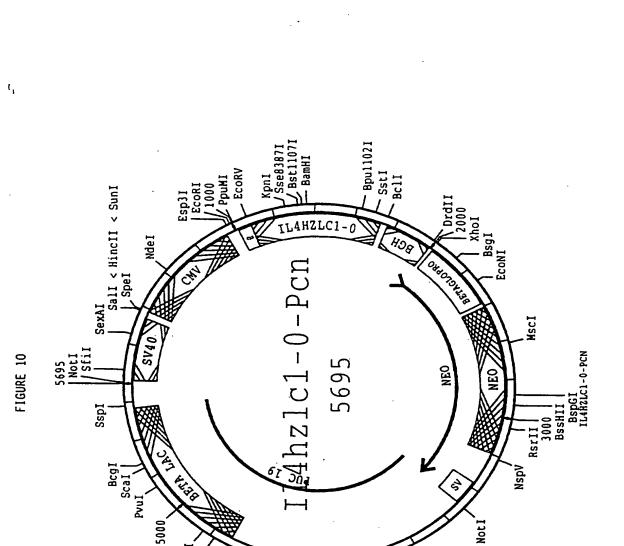




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